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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/371,347	08/10/1999	ROY A. GRAVEL	50004/003003	9130

7590

05/31/2002

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EXAMINER

STEADMAN, DAVID J

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 05/31/2002

20

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application No.

09/371,347

Applicant(s)

GRAVEL ET AL.

Examiner

David J. Steadman

Art Unit

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 20 May 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY [check either a) or b)]**

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 20 May 2002. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☒ The proposed amendment(s) will not be entered because:
- (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☒ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: see attachment.

3. ☒ Applicant's reply has overcome the following rejection(s): see attachment.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attachment.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☒ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: NONE.

Claim(s) objected to: NONE.

Claim(s) rejected: 1-5 and 35-47.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

8. ☐ The proposed drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.
10. ☐ Other: \_\_\_\_\_.

**ADVISORY ACTION**

1. Claims 1-5 and 35-47 are pending in the application.
2. Claims 1-5 and 35-47 are rejected.
3. No claim(s) is/are in condition for allowance.
4. The after-final amendment to claims 3, 36-38, and 41-43 in Paper No. 05/20/02 has not been entered because said amendment presents new issues requiring further search necessitating new literature, patent, and sequence searches. In particular, claims 48 and 49 introduce claims reciting sequences that have not been presented for examination prior to the filing of the after-final amendment. Also, the after-final amendment presents new claims without canceling a corresponding number of finally-rejected claims. See MPEP 714.13 regarding non-entry of an after-final amendment.
5. The request for reconsideration has been considered but does not place the case in condition for allowance for the reasons discussed below.
6. Rejection of claim 3 under 35 USC 112, second paragraph as being confusing is maintained. Applicants argue the claim has been amended to recite "respectively" following "SEQ ID NO:48". The amendment would appear to overcome the rejection. However, in view of non-entry of the amendment, the rejection is maintained for the reasons of record.
7. Rejection of claim 47 under 35 USC 112, second paragraph as being indefinite in the recitation of "a consensus binding site for one or more cofactors" is maintained. The rejection was fully explained in a previous Office action. Applicants argue that a skilled artisan can readily identify a consensus binding site for FAD, FMN, and/or NADPH. In support of applicants' assertion, applicants have provided a Declaration by applicant Gravel asserting that one of skill in the art can readily identify a consensus binding site for FAD, FMN, and/or NADPH. Applicants have also submitted Appendices A and B in support of the assertion that a skilled artisan can readily identify a consensus binding site for FAD, FMN, and/or NADPH. Applicants' arguments, Declaration, and Appendices have been fully considered, but are not found persuasive to overcome the rejection. As can be seen in Figure 6 of Appendix A (Wang et al. *Proc Natl Acad Sci USA* 94:8411-8416) and Appendix B, which appears to be an enlargement of Figure 6 of Wang

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et al. and not Figure 6 of the instant specification as stated by applicants, there is *significant* sequence variation within the FAD, FMN, and NADPH consensus binding sites. Therefore, it is unclear as to the residues of the consensus sequence that are encompassed within the scope of the claim. The rejection is maintained for the reasons of record.

8. Rejection of claims 1, 2, 4, 5, and 35-47 under 35 U.S.C. 112, first paragraph, as lacking written description is maintained. The rejection was fully explained in a previous Office action.

Addressing the rejection of claims 1, 2, and 45-47 as lacking adequate structural description, applicants argue that the specification discloses polynucleotide sequences (SEQ ID NOs:1, 41, 43, 45, and 47) encoding mammalian methionine synthase reductase (MSR) polypeptides and distinguishing characteristics to sufficiently characterize polynucleotides encoding such that one of skill in the art could identify a mammalian MSR polynucleotide. Applicants argue such mammalian MSR polynucleotides can be identified using sequence homology based on invariant amino acids between the amino acid sequences of human and C. elegans MSR polypeptides and conserved regions of FAD, FMN, and NADPH binding. Applicants argue that MSR polynucleotides can also be identified using disclosed enzymatic assays.

Addressing the rejection of claims 4, 5, and 35-47 as lacking adequate functional description, Applicants argue three species of the claimed genus of polynucleotides that hybridize to SEQ ID NOs:1 or 41 have been disclosed in the specification as SEQ ID NOs:43, 45, or 47, oligonucleotides listed in Table 1, complementary and antisense polynucleotides and provides guidance for making such polynucleotides.

Applicants' arguments have been fully considered but are not found persuasive to overcome the rejection. As stated in a previous Office action, other than the polynucleotide sequences of SEQ ID NOs:1, 41, 43, 45, and 47, which are human MSR polynucleotides, applicants have not disclosed the structures of any other polynucleotides encoding mammalian MSR polypeptides. Also stated in a previous Office action, applicants have provided no functional description of the genus of claimed polynucleotides. The rejection is maintained for the reasons of record.

9. The enablement rejection of claims 1, 2, 4, 5, and 35-47 under 35 U.S.C. 112, first paragraph, is maintained. The rejection was fully explained in a previous Office action.

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Applicants argue the claimed polynucleotides are fully enabled by the instant specification.

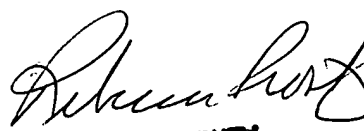
Applicants argue the applicants disclosure of the human MSR polynucleotides of SEQ ID NOs:1, 41, 43, 45, and 47 enables one of skill in the art to identify any other human MSR polynucleotide. It is noted that applicants claimed polynucleotides are not so limited to human MSR polynucleotides.

Applicants argue that provided the sequences of SEQ ID NOs:1, 41, 43, 45, and 47, one of skill in the art can design primers or probes to make other mammalian MSR polynucleotides. Applicants argue MSR polynucleotides can be screened using an MSR enzyme assay as disclosed in the instant specification. Applicants argue that the claimed polynucleotides are not limited to those encoding polypeptides with MSR enzyme activity. Applicants argue such polynucleotides have use in diagnostic assays and antisense inhibition of MSR expression.

Applicants' argument has been fully considered but is not found persuasive to overcome the rejection. As stated in a previous Office action, applicants have not provided guidance as to how of skill in the art can make and use *all* of the claimed polynucleotides, broadly including fragments, variants, and polynucleotides encoding polypeptides with and without MSR activity. Undue experimentation would therefore be required to make and use the claimed polynucleotides. The rejection is maintained for the reasons of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The examiner can normally be reached Monday-Friday from 8:00 am to 4:30 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for this Art Unit is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.

  
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